Risk factors for rectal colonization with vancomycin-resistant enterococci in Shiraz, Iran

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Summary

Objectives: In order to determine the risk factors for rectal colonization with vancomycin-resistant enterococci (VRE) at the Shiraz Namazi Hospital, we performed a nested case—control study.
Methods: From December 2003 to July 2004 rectal swabs were taken from 700 randomly selected hospitalized patients every 5 days.
Results: A total of 99 of the 700 patients (14%) were colonized with VRE (cases) and 59 patients were colonized with vancomycin-sensitive strains (VSE), serving as controls. In the univariate analysis, history of antibiotic use ($p = 0.04$), underlying disease ($p = 0.013$), hemodialysis ($p = 0.03$), use of third generation cephalosporins ($p = 0.04$), use of vancomycin ($p = 0.04$), and duration of vancomycin therapy longer than 7 days ($p = 0.02$) were significantly associated with VRE colonization. In a multivariate analysis, underlying disease and the duration of vancomycin use longer than 7 days were independently associated with VRE colonization.
Conclusion: Our study, the first on VRE carriage in Iran, demonstrates that VRE prevalence is high in Shiraz and confirms earlier observations in other countries. The identified risk factor 'use of vancomycin longer than 7 days' may be avoidable, indicating a feasible intervention strategy in the control of VRE.

Introduction

The worldwide observed increase in antimicrobial resistance among pathogens causing nosocomial infections constitutes a major public health problem.[1] One of the best examples of the bacterial quest for survival are enterococci. For years viewed as harmless inhabitants of the intestinal flora, enterococci have acquired resistance to multiple antibiotics, making glycopeptides like vancomycin one of the last available compounds for therapy. Vancomycin-resistant enterococci (VRE) are among the most feared pathogens in hospitals in the USA. However, the epidemiology of VRE in Europe and America appears to be very different. In contrast to the

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alarming situation in hospitals in the USA, infections due to VRE remain uncommon in Europe.[2] The US National Nosocomial Infection Surveillance (NNIS) system has revealed a significant increase in the percentage of nosocomial *Enterococcus spp* strains displaying vancomycin resistance. The figure for the incidence of VRE in intensive care unit (ICU) patients rose from 0.4% in 1989 to 23.4% in 1997. In non-ICU patients, the percentage increased from 0.3% to 15.4%, representing a 50-fold increase in a relatively short time span.[3] According to data from the NNIS system, enterococci are now the fourth leading cause of nosocomial infections and the third in ICU patients in the USA.[1,4,5]

Risk factors for VRE colonization may be patient-, hospital-, environment-, and antibiotic-related.[1] Although many studies have been performed in Europe and the USA on the prevalence, incidence, epidemiology, and risk factors of VRE, data for the Middle East and Asia are scarce.[6] This study is the first investigation on the epidemiology of VRE in Iran. The aim of the present study was to determine the prevalence and risk factors of rectal colonization with VRE in Iranian patients.

Materials and methods

Setting

The study hospital (Shiraz Namazi Hospital) provides primary and tertiary care in a 750-bed health facility for patients admitted from Shiraz, Fars State and other southern states of Iran. Twenty-five wards participated in this study, including nine ICUs with a total capacity of 50 beds (two neurosurgical ICUs, two medical ICUs, one surgical ICU, one pediatric ICU, one neonatal ICU, and two cardiac care units), five surgical wards with a total of 120 beds (neurosurgery, plastic surgery, general surgery, urology, and trauma), seven medical wards with a total of 135 beds (one cardiology, one female medical ward, one male medical ward, two general medical wards, and two oncology wards), and four pediatric wards with a total capacity of 80 beds (three medical wards and one surgical ward).

Currently, there are no VRE-specific infection control strategies implemented in the investigated hospital, and no screening policy or surveillance concepts. There are, however, general measures including hand hygiene and standard precaution concepts, although compliance varies.

Patients

All hospitalized patients admitted during the study period (December 2003 through July 2004) with a hospital stay of longer than 5 days (700 patients) were selected for this study.

Study design

This study was designed as a nested case—control and descriptive-analytic study to determine the prevalence and risk factors of colonization with VRE. Educated nurses took serial rectal swabs every 5 days. Samples were sent to the laboratory in transportation tubes (Venturi Transystem, Copan Diagnostics Inc., New York, NY, USA). A case patient was defined as any patient who had a positive sample yielding VRE; a control patient was a patient from whom vancomycin-sensitive enterococci (VSE) were yielded. A third group encompassed all patients with repetitive negative *Enterococcus spp* samples.

Data collection

Data from each patient were extracted from the medical records and at the bedside. Obtained data included the following: age, sex, co-morbidity and underlying disease, ward of admission, duration of stay, prior admission, prior antibiotic use, clinical outcome, kind and duration of antibiotic use before colonization, and laboratory results.

Microbiological methods

Rectal swab specimens were cultivated on a selective agar and incubated at 37 °C overnight. Cephalexin—aztreonam—arabinose agar (CAA) was prepared by adding 40 g of Columbia agar base (Unipath, Basingstoke, UK), 10 g of arabinose (Sigma Chemical Co., Poole, UK), and 3.6 ml of phenol-red (2%; BDH, Lutterworth, UK) to 1 liter of de-ionized water. The medium was mixed and the pH was adjusted to 7.8. The agar was autoclaved at 114 °C for 20 min. Fresh sterile solutions of aztreonam (Bristol-Myers Squibb, Hounslow, UK) and cephalexin (Sigma) were added to give final concentrations of 75 mg/l and 50 mg/l, respectively.[7]

Swabs were streaked on the surface of CAA. The plates were incubated at 37 °C in air for 24 h and examined for growth and fermentation of arabinose. A change in the color of the medium surrounding the colony, from red to yellow, indicated arabinose fermentation.

Conventional organism identification and susceptibility testing

Red to yellow colonies resembling enterococci on the CAA plates were further identified by conventional laboratory methods, including Gram staining and determination of colonial morphology and biochemical and growth characteristics.[8,9] Species identification was performed using API 20 STREP (bioMerieux, Marcy L'Etoile, France). In vitro susceptibility to ampicillin, penicillin, gentamicin, vancomycin, and teicoplanin was tested according to Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS)[10] guidelines, using the agar dilution method and Mueller—Hinton agar (Becton Dickinson, Franklin Lakes, USA).

Definitions

The presence of the following conditions was documented for underlying disease: immunosuppression, neutropenia, renal failure (as indicated by baseline creatinine level of >0.2 mg/dl), hemodialysis, cancer, diabetes mellitus, major surgery, severe cardiac disease (as indicated by cardiac heart failure and myocardial infarction), sepsis, and systemic lupus erythematosus (SLE). Prior admission was defined as admission during the six months before the present hospitalization. Prior antibiotic use was defined as the administration of antimicrobials for >72 h during the 60 days before the onset of hospitalization. Duration of antibiotic use before coloniza-